AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions, and listings, of claims in the application.

1. (Currently Amended) A method of producing a stable, sterile pharmaceutical formulation comprising lyophilized tobramycin, which method comprises:

(a) preparing a liquid composition comprising tobramycin and a solvent ~~which comprises alcohol,~~ comprising about 4.5% by volume or less of tert-butyl alcohol,

(b) freezing the composition to a temperature of from about -10° C to about -70° C, to produce a frozen mixture, wherein the temperature is maintained for from at least about 1 hour to about 30 hours,

(c) subjecting the frozen mixture to a primary drying stage, which comprises applying a vacuum to reduce the pressure to about 100 micron Hg, and, while applying the vacuum, changing the temperature of the frozen mixture to a primary drying temperature of from about -15° C to about 20° C, wherein the temperature of the frozen mixture in the primary drying stage is changed at a rate of from about 0.1° C to about 0.5° C per minute, and wherein the primary drying temperature is maintained for at least about 40 hours to about 80 hours, to produce a first intermediate, and

(d) subjecting the first intermediate to a secondary drying stage, which comprises applying a vacuum to reduce the pressure to about 100 micron Hg, and, while applying the vacuum, changing the temperature of the frozen mixture to a secondary drying temperature of from about 30° C to about 45° C, wherein the temperature of the frozen mixture in the secondary drying stage is changed at a rate of from about 0.1° C to about 0.5° C per minute, and wherein the secondary drying temperature is maintained for at least about 5 hours to about 30 hours, to produce the pharmaceutical formulation, wherein the lyophilized tobramycin is in the form of a free-flowing powder.

2. (Original) The method of claim 1, wherein the composition is frozen to a temperature of from about -45° C to about -60° C.

3. (Original) The method of claim 1, wherein the composition is frozen to a temperature of about -45° C.

4. (Original) The method of claim 1, wherein the primary drying temperature is from about -15° C to about 10° C.

5. (Original) The method of claim 1, wherein the temperature at which the composition is frozen is held for at least about 10 hours to about 20 hours.

6. (Original) The method of claim 1, wherein the temperature of the frozen mixture in the primary drying stage is raised at a rate of about 0.1° C per minute.

7. (Original) The method of claim 1, wherein the primary drying temperature in the primary drying stage is maintained for at least about 60 hours to about 70 hours.

8. (Original) The method of claim 1, wherein the primary drying temperature in the primary drying stage is maintained until the temperature of the frozen mixture is about equal to the primary drying temperature.

9. (Original) The method of claim 1, wherein the secondary drying temperature is from about 30 °C to about 40° C.

10. (Original) The method of claim 1, wherein the temperature of the frozen mixture in the secondary drying stage is raised at a rate of about 0.2° C per minute.

11. (Original) The method of claim 1, wherein the secondary drying temperature in the secondary drying stage is maintained for at least about 10 hours to about 20 hours.

12. (Original) The method of claim 1, wherein the secondary drying temperature in the secondary drying stage is held until the moisture content is about 1.0 wt% of the formulation.

13. (Original) The method of claim 1, wherein (a) the primary drying temperature is from about -15° C to about -10° C, (b) the temperature of the frozen mixture in the primary

drying stage is raised at a rate of about 0.1° C per minute, and (c) the primary drying temperature is maintained for at least about 60 hours to about 70 hours.

14. (Original) The method of claim 1, wherein (a) the composition is frozen to a temperature of from about -45° C to about -60° C, and the temperature at which the composition is frozen is maintained for at least about 10 hours to 20 hours, (b) the primary drying temperature is from about -15° C to about -10° C, and the primary drying temperature is maintained for at least about 60 hours to about 70 hours, and (c) the secondary drying temperature is from about 30° C to about 40 °C, and the secondary drying temperature is maintained for at least about 10 hours to about 20 hours.

~~16.~~ 15. (Currently Amended) The method of claim 1, wherein (a) the composition is frozen to a temperature of about -48° C, and the temperature at which the composition is frozen is maintained for at least about 15 hours, (b) the primary drying temperature is about -15° C, and the primary drying temperature is maintained for at least about 67 hours, and (c) the secondary drying temperature is about 30° C, and the secondary drying temperature is maintained for at least about 15 hours.

16. (Canceled)

17. (Original) A stable, sterile pharmaceutical formulation comprising lyophilized tobramycin, wherein the formulation is produced by the method of claim 1.

18. (Original) The formulation of claim 17, wherein the lyophilized tobramycin is present in an amount of from about 0.5 grams to about 5.0 grams.

19. (Original) The formulation of claim 17, wherein the lyophilized tobramycin is present in an amount of about 1.2 grams.

20. (Currently Amended) The formulation of claim 17, wherein the ~~alcohol is tert-butyl alcohol, and the~~ lyophilized tobramycin contains less than about 1.1% of tert-butyl alcohol.

21. (Original) The formulation of claim 17, contained within a sealed container.

22. (Original) The formulation of claim 21, wherein the container has a volume of about 50 mL, and about 1.2 g of lyophilized tobramycin are contained within the container.

23. (Original) The formulation of claim 22, wherein the container defines an opening and comprises a means for sealing the opening.

24. (Original) The formulation of claim 23, wherein the container is a glass vial.

25. (Original) The formulation of claim 23, wherein the means for sealing the opening comprises a stopper.

26. (Original) The formulation of claim 25, wherein the stopper is pierceable by a hypodermic needle or a blunt cannula.

27. (Original) The formulation of claim 25, further comprising an outer seal which covers and entirely surrounds the stopper.

28. (Original) The formulation of claim 27, wherein the outer seal comprises a lid which is manually removable, to provide access to the stopper.

29. (Original) A solution prepared by dissolving the formulation of claim 17 in an aqueous vehicle.

30. (Original) The solution of claim 29, wherein the tobramycin is present in the solution in an amount of about 40 mg/mL or less.

31. (Original) The solution of claim 29, wherein the tobramycin is present in the solution in an amount of about 2 mg/mL or less.

32. (Original) The solution of claim 29, wherein the tobramycin is present in the solution in an amount of from about 0.2 mg/mL to about 2 mg/mL.

33.-37. (Canceled)

38. (Original) A pharmaceutical dosage form comprising a sealed container and a pharmaceutical formulation comprising a therapeutically effective amount of lyophilized

tobramycin contained within the container, wherein the lyophilized tobramycin is in the form of a free-flowing powder, and is produced by the method of claim 1.

39. (Original) The pharmaceutical dosage form of claim 38, wherein the lyophilized tobramycin is present in the sealed container in an amount from about 0.5 grams to about 5 grams.

40. (Original) The pharmaceutical dosage form of claim 39, wherein the lyophilized tobramycin is present in the sealed container in an amount of about 1.2 grams.

41. (Original) A method of treating a disease in a patient, which method comprises dissolving the pharmaceutical formulation of claim 17 in a pharmaceutically acceptable solvent to produce a pharmaceutically acceptable solution, and administering the solution to a patient in need thereof.

42. (Original) The method of claim 41, wherein the disease is caused by a microorganism.

43. (Original) The method of claim 42, wherein the microorganism is selected from the group consisting of *P. aeruginosa*, *Proteus* sp., *P. mirabilis*, *M. morganii*, *P. rettgeri*, *P. vulgaris*, *E. coli*, Klebsiella-Enterobacter-Serratia group, *Citrobacter* sp., *Providencia* sp., *Staphylococci*, and *S. aureus*.

44. (Original) The method of claim 41, wherein the disease is selected from the group consisting of septicemia, complicated and recurrent urinary tract infections, lower respiratory infections, skin and soft tissue infections, burns, peritonitis, and central nervous system infections.